EMA/477307/2010

European Medicines Agency decision

P/156/2010

of 27 August 2010

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for ivabradine hydrochloride (Corlentor), (EMEA-000627-PIP01-09) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This Decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8670
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for ivabradine hydrochloride (Corlentor), (EMEA-000627-PIP01-09) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Les Laboratoires Servier on 10 July 2009 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 16 July 2010, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation and Article 13 of said Regulation,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

A paediatric investigation plan for ivabradine hydrochloride (Corlentor), film-coated tablet, solution for injection, oral solution, intravenous use, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for ivabradine hydrochloride (Corlentor), film-coated tablet, solution for injection, oral solution, intravenous use, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for ivabradine hydrochloride (Corlentor), film-coated tablet, solution for injection, oral solution, intravenous use, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to Les Laboratoires Servier, 22, rue Garnier, 92578 Neuilly-sur-Seine, France.

Done at London, 27 August 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

EMA/PDCO/409946/2010

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-000627-PIP01-09

Scope of the application

Active substance(s):

Ivabradine hydrochloride

Invented name:

Corlentor

Condition(s):

Coronary artery disease

Angina pectoris

Chronic heart failure

Reduction of heart rate during Multislice Computed Tomography Coronary Angiography (MSCT CA)

Pharmaceutical form(s):

Film-coated tablet

Solution for injection

Oral solution

Route(s) of administration:

Intravenous use

Oral use

Name/corporate name of the PIP applicant:

Les Laboratoires Servier

Information about the authorised medicinal product: see Annex II

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Les Laboratoires Servier submitted for agreement to the European Medicines Agency on 10 July 2009 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 20 August 2009.

Supplementary information was provided by the applicant on 22 April 2010.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 18 of said Regulation,
   - to grant a deferral in accordance with Article 21 of said Regulation,
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

London, 16 July 2010

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman

(Signature on file)

Annex I

The measures and timelines of the agreed Paediatric Investigation Plan and the subset(s) of the paediatric population and condition(s) covered by the waiver

1. Condition(s)

Coronary artery disease

Angina pectoris

Chronic heart failure

Reduction of heart rate during Multislice Computed Tomography Coronary Angiography (MSCT CA)

2. Waiver

2.1. Condition

Coronary artery disease

The waiver applies to:

- All subsets of the paediatric population from birth to less than 18 years of age
- for film-coated tablet for oral use, for solution for injection for intravenous use and for oral solution for oral use
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2.2. Condition

Angina pectoris

The waiver applies to:

- All subsets of the paediatric population from birth to less than 18 years of age
- for film-coated tablet for oral use, for solution for injection for intravenous use and for oral solution for oral use
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2.3. Condition

Chronic heart failure

The waiver applies to:

- Neonates and infants from birth to less than 6 months of age
- for film-coated tablet for oral use, for solution for injection for intravenous use and for oral solution for oral use
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2.4. Condition

Reduction of heart rate during Multislice Computed Tomography Coronary Angiography (MSCT CA)

The waiver applies to:

- Neonates and infants from birth to less than 2 years of age
- for film-coated tablet for oral use, for solution for injection for intravenous use and for oral solution for oral use
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

3. Paediatric Investigation Plan

3.1. Condition to be investigated

Chronic heart failure

3.1.1. Indication targeted by the PIP

Treatment of chronic heart failure

3.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 6 months to less than 18 years of age.

3.1.3. Pharmaceutical form(s)

Oral solution for oral use

3.1.4. Studies

Area	**Number of studies**	**Description**
Quality	0	Not applicable
Non-clinical	0	Not applicable
Clinical	2	Study 1: A monocentre, open-label, randomised, two-period, cross-over bioavailability study in healthy male volunteers to support the paediatric formulation development (PKH-16257-086) Study 2: A randomised, double-blind, placebo controlled, multicentre PK/PD and dose-finding study in children from 6 months to less than 18 years of age with chronic heart failure (CL2-16257-090)

3.2. Condition to be investigated

Reduction of heart rate during Multislice Computed Tomography Coronary Angiography (MSCT CA)

3.2.1. Indication targeted by the PIP

Reduction of heart rate during Multislice Computed Tomography Coronary Angiography (MSCT CA)

3.2.2. Subset(s) of the paediatric population concerned by the paediatric development

From 2 to less than 18 years of age.

3.2.3. Pharmaceutical form(s)

Solution for injection for intravenous use

3.2.4. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	3	Study 1: A preliminary 4-week toxicity study by oral route (gavage) in juvenile Wistar rats (35438 RSR – TOX-16257-040-FRA) Study 2: A preliminary 2 or 4-week toxicity study by oral route (gavage) in juvenile Wistar rats (35658 EPR – PF-09-16257-168-RRTK) Study 3: A 10-week toxicity study by oral route (gavage) in juvenile Wistar rats followed by a 3-week recovery period (35439 RSR – TOX-16257-042-FRA)
Clinical	1	Study 4: A double blind, non-randomised multicentre, non-controlled PK/PD and dose-finding study in children from 2 to less than 18 years of age undergoing MSCT-CA examination (CL2-16257-085)

4. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety issues or efficacy in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By September 2013
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

EU Number	Invented Name	Strength	Pharmaceutical form	Route of administration	Packaging	Package size
EU/1/05/317/001	Corlentor	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	14 tablets
EU/1/05/317/002	Corlentor	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	28 tablets
EU/1/05/317/003	Corlentor	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	56 tablets
EU/1/05/317/004	Corlentor	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	84 tablets
EU/1/05/317/005	Corlentor	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	98 tablets
EU/1/05/317/006	Corlentor	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	100 tablets
EU/1/05/317/007	Corlentor	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	112 tablets
EU/1/05/317/008	Corlentor	7.5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	14 tablets
EU/1/05/317/009	Corlentor	7.5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	28 tablets
EU/1/05/317/010	Corlentor	7.5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	56 tablets
EU/1/05/317/011	Corlentor	7.5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	84 tablets
EU/1/05/317/012	Corlentor	7.5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	98 tablets
EU/1/05/317/013	Corlentor	7.5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	100 tablets
EU/1/05/317/014	Corlentor	7.5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	112 tablets